SEQUENCE LISTING

<110> WADA, Naoya
OKAMOTO, Takashi
TANIGAKI, Keiji
DOI, Hirofumi
KIKUCHI, Yasuhiro
IMAI, Kensaku

<120> Method for Inhibiting Telomerase Activity and Inhibitor Thereof

<130> 3190-087

<140> US Unassigned
<141> 2005-12-29

<150> JP P2004-143902
<151> 2004-05-13

<150> PCT/JP2005/008239
<151> 2005-04-28

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<170> PatentIn version 3.1

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gtt gca ccc ggc gga ccc ggc ttg ggc ggt gct ccg ggg ggg cgg cgg       96
Val Ala Pro Gly Gly Pro Gly Leu Gly Gly Ala Pro Gly Gly Arg Arg
            20                  25                  30

gag ccc aag aag tac gca gtg acc gac gac tac cag ttg tcc aag cag      144
Glu Pro Lys Lys Tyr Ala Val Thr Asp Asp Tyr Gln Leu Ser Lys Gln
        35                  40                  45

gtg ctg ggc ctg ggt gtg aac ggc aaa gtg ctg gag tgc ttc cat cgg      192
Val Leu Gly Leu Gly Val Asn Gly Lys Val Leu Glu Cys Phe His Arg
    50                  55                  60

cgc act gga cag aag tgt gcc ctg aag ctc ctg tat gac agc ccc aag      240
Arg Thr Gly Gln Lys Cys Ala Leu Lys Leu Leu Tyr Asp Ser Pro Lys
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Ile Val Cys Ile Leu Asp Val Tyr Glu Asn Met His His Gly Lys Arg
            100                 105                 110

tgt ctc ctc atc atc atg gaa tgc atg gaa ggt ggt gag ttg ttc agc      384
Cys Leu Leu Ile Ile Met Glu Cys Met Glu Gly Gly Glu Leu Phe Ser
        115                 120                 125

agg att cag gag cgt ggc gac cag gct ttc act gag aga gaa gct gca      432
Arg Ile Gln Glu Arg Gly Asp Gln Ala Phe Thr Glu Arg Glu Ala Ala
    130                 135                 140

gag ata atg cgg gat att ggc act gcc atc cag ttt ctg cac agc cat      480
Glu Ile Met Arg Asp Ile Gly Thr Ala Ile Gln Phe Leu His Ser His
145                 150                 155                 160

aac att gcc cac cga gat gtc aag cct gaa aac cta ctc tac aca tct      528
Asn Ile Ala His Arg Asp Val Lys Pro Glu Asn Leu Leu Tyr Thr Ser
                165                 170                 175

aag gag aaa gac gca gtg ctt aag ctc acc gat ttt ggc ttt gct aag      576
Lys Glu Lys Asp Ala Val Leu Lys Leu Thr Asp Phe Gly Phe Ala Lys
            180                 185                 190

gag acc acc caa aat gcc ctg cag aca ccc tgc tat act ccc tat tat      624
Glu Thr Thr Gln Asn Ala Leu Gln Thr Pro Cys Tyr Thr Pro Tyr Tyr
        195                 200                 205

gtg gcc cct gag gtc ctg ggt cca gag aag tat gac aag tca tgt gac      672
Val Ala Pro Glu Val Leu Gly Pro Glu Lys Tyr Asp Lys Ser Cys Asp
    210                 215                 220

atg tgg tcc ctg ggt gtc atc atg tac atc ctc ctt tgt ggc ttc cca      720
Met Trp Ser Leu Gly Val Ile Met Tyr Ile Leu Leu Cys Gly Phe Pro
225                 230                 235                 240

ccc ttc tac tcc aac acg ggc cag gcc atc tcc ccg ggg atg aag agg      768
Pro Phe Tyr Ser Asn Thr Gly Gln Ala Ile Ser Pro Gly Met Lys Arg
                245                 250                 255

agg att cgc ctg ggc cag tac ggc ttc ccc aat cct gag tgg tca gaa      816
Arg Ile Arg Leu Gly Gln Tyr Gly Phe Pro Asn Pro Glu Trp Ser Glu
            260                 265                 270

gtc tct gag gat gcc aag cag ctg atc cgc ctc ctg ttg aag aca gac      864
Val Ser Glu Asp Ala Lys Gln Leu Ile Arg Leu Leu Leu Lys Thr Asp
        275                 280                 285

ccc aca gag agg ctg acc atc act cag ttc atg aac cac ccc tgg atc      912
Pro Thr Glu Arg Leu Thr Ile Thr Gln Phe Met Asn His Pro Trp Ile
    290                 295                 300

aac caa tcg atg gta gtg cca cag acc cca ctc cac acg gcc cga gtg      960
Asn Gln Ser Met Val Val Pro Gln Thr Pro Leu His Thr Ala Arg Val
305                 310                 315                 320

ctg cag gag gac aaa gac cac tgg gac gaa gtc aag gag gag atg acc     1008
Leu Gln Glu Asp Lys Asp His Trp Asp Glu Val Lys Glu Glu Met Thr
                325                 330                 335
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agt gcc ttg gcc act atg cgg gta gac tac gac cag gtg aag atc aag     1056
Ser Ala Leu Ala Thr Met Arg Val Asp Tyr Asp Gln Val Lys Ile Lys
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gac ctg aag acc tct aac aac cgg ctc ctc aac aag agg aga aaa aag     1104
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        355                 360                 365

cag gca ggc agc tcc tct gcc tca cag ggc tgc aac aac cag tag         1149
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        35                  40                  45

Val Leu Gly Leu Gly Val Asn Gly Lys Val Leu Glu Cys Phe His Arg
    50                  55                  60

Arg Thr Gly Gln Lys Cys Ala Leu Lys Leu Leu Tyr Asp Ser Pro Lys
65                  70                  75                  80

Ala Arg Gln Glu Val Asp His His Trp Gln Ala Ser Gly Gly Pro His
                85                  90                  95

Ile Val Cys Ile Leu Asp Val Tyr Glu Asn Met His His Gly Lys Arg
            100                 105                 110

Cys Leu Leu Ile Ile Met Glu Cys Met Glu Gly Gly Glu Leu Phe Ser
        115                 120                 125

Arg Ile Gln Glu Arg Gly Asp Gln Ala Phe Thr Glu Arg Glu Ala Ala
    130                 135                 140

Glu Ile Met Arg Asp Ile Gly Thr Ala Ile Gln Phe Leu His Ser His
145                 150                 155                 160

Asn Ile Ala His Arg Asp Val Lys Pro Glu Asn Leu Leu Tyr Thr Ser
                165                 170                 175
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Lys Glu Lys Asp Ala Val Leu Lys Leu Thr Asp Phe Gly Phe Ala Lys
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Glu Thr Thr Gln Asn Ala Leu Gln Thr Pro Cys Tyr Thr Pro Tyr Tyr
        195                 200                 205

Val Ala Pro Glu Val Leu Gly Pro Glu Lys Tyr Asp Lys Ser Cys Asp
    210                 215                 220

Met Trp Ser Leu Gly Val Ile Met Tyr Ile Leu Leu Cys Gly Phe Pro
225                 230                 235                 240

Pro Phe Tyr Ser Asn Thr Gly Gln Ala Ile Ser Pro Gly Met Lys Arg
                245                 250                 255

Arg Ile Arg Leu Gly Gln Tyr Gly Phe Pro Asn Pro Glu Trp Ser Glu
            260                 265                 270

Val Ser Glu Asp Ala Lys Gln Leu Ile Arg Leu Leu Leu Lys Thr Asp
        275                 280                 285

Pro Thr Glu Arg Leu Thr Ile Thr Gln Phe Met Asn His Pro Trp Ile
    290                 295                 300

Asn Gln Ser Met Val Val Pro Gln Thr Pro Leu His Thr Ala Arg Val
305                 310                 315                 320

Leu Gln Glu Asp Lys Asp His Trp Asp Glu Val Lys Glu Glu Met Thr
                325                 330                 335

Ser Ala Leu Ala Thr Met Arg Val Asp Tyr Asp Gln Val Lys Ile Lys
            340                 345                 350

Asp Leu Lys Thr Ser Asn Asn Arg Leu Leu Asn Lys Arg Arg Lys Lys
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Gln Ala Gly Ser Ser Ser Ala Ser Gln Gly Cys Asn Asn Gln
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1               5                   10                  15

cac tac cgc gag gtg ctg ccg ctg gcc acg ttc gtg cgg cgc ctg ggg       96
His Tyr Arg Glu Val Leu Pro Leu Ala Thr Phe Val Arg Arg Leu Gly
            20                  25                  30

ccc cag ggc tgg cgg ctg gtg cag cgc ggg gac ccg gcg gct ttc cgc      144
Pro Gln Gly Trp Arg Leu Val Gln Arg Gly Asp Pro Ala Ala Phe Arg
        35                  40                  45

gcg ctg gtg gcc cag tgc ctg gtg tgc gtg ccc tgg gac gca cgg ccg      192
Ala Leu Val Ala Gln Cys Leu Val Cys Val Pro Trp Asp Ala Arg Pro
    50                  55                  60

ccc ccc gcc gcc ccc tcc ttc cgc cag gtg tcc tgc ctg aag gag ctg      240
Pro Pro Ala Ala Pro Ser Phe Arg Gln Val Ser Cys Leu Lys Glu Leu
65                  70                  75                  80

gtg gcc cga gtg ctg cag agg ctg tgc gag cgc ggc gcg aag aac gtg      288
Val Ala Arg Val Leu Gln Arg Leu Cys Glu Arg Gly Ala Lys Asn Val
                85                  90                  95

ctg gcc ttc ggc ttc gcg ctg ctg gac ggg gcc cgc ggg ggc ccc ccc      336
Leu Ala Phe Gly Phe Ala Leu Leu Asp Gly Ala Arg Gly Gly Pro Pro
            100                 105                 110

gag gcc ttc acc acc agc gtg cgc agc tac ctg ccc aac acg gtg acc      384
Glu Ala Phe Thr Thr Ser Val Arg Ser Tyr Leu Pro Asn Thr Val Thr
        115                 120                 125

gac gca ctg cgg ggg agc ggg gcg tgg ggg ctg ctg ctg cgc cgc gtg      432
Asp Ala Leu Arg Gly Ser Gly Ala Trp Gly Leu Leu Leu Arg Arg Val
    130                 135                 140

ggc gac gac gtg ctg gtt cac ctg ctg gca cgc tgc gcg ctc ttt gtg      480
Gly Asp Asp Val Leu Val His Leu Leu Ala Arg Cys Ala Leu Phe Val
145                 150                 155                 160

ctg gtg gct ccc agc tgc gcc tac cag gtg tgc ggg ccg ccg ctg tac      528
Leu Val Ala Pro Ser Cys Ala Tyr Gln Val Cys Gly Pro Pro Leu Tyr
                165                 170                 175

cag ctc ggc gct gcc act cag gcc cgg ccc ccg cca cac gct agt gga      576
Gln Leu Gly Ala Ala Thr Gln Ala Arg Pro Pro Pro His Ala Ser Gly
            180                 185                 190

ccc cga agg cgt ctg gga tgc gaa cgg gcc tgg aac cat agc gtc agg      624
Pro Arg Arg Arg Leu Gly Cys Glu Arg Ala Trp Asn His Ser Val Arg
        195                 200                 205

gag gcc ggg gtc ccc ctg ggc ctg cca gcc ccg ggt gcg agg agg cgc      672
Glu Ala Gly Val Pro Leu Gly Leu Pro Ala Pro Gly Ala Arg Arg Arg
    210                 215                 220

ggg ggc agt gcc agc cga agt ctg ccg ttg ccc aag agg ccc agg cgt      720
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Gly Gly Ser Ala Ser Arg Ser Leu Pro Leu Pro Lys Arg Pro Arg Arg
225                 230                 235                 240

ggc gct gcc cct gag ccg gag cgg acg ccc gtt ggg cag ggg tcc tgg      768
Gly Ala Ala Pro Glu Pro Glu Arg Thr Pro Val Gly Gln Gly Ser Trp
                245                 250                 255

gcc cac ccg ggc agg acg cgt gga ccg agt gac cgt ggt ttc tgt gtg      816
Ala His Pro Gly Arg Thr Arg Gly Pro Ser Asp Arg Gly Phe Cys Val
            260                 265                 270

gtg tca cct gcc aga ccc gcc gaa gaa gcc acc tct ttg gag ggt gcg      864
Val Ser Pro Ala Arg Pro Ala Glu Glu Ala Thr Ser Leu Glu Gly Ala
        275                 280                 285

ctc tct ggc acg cgc cac tcc cac cca tcc gtg ggc cgc cag cac cac      912
Leu Ser Gly Thr Arg His Ser His Pro Ser Val Gly Arg Gln His His
    290                 295                 300

gcg ggc ccc cca tcc aca tcg cgg cca cca cgt ccc tgg gac acg cct      960
Ala Gly Pro Pro Ser Thr Ser Arg Pro Pro Arg Pro Trp Asp Thr Pro
305                 310                 315                 320

tgt ccc ccg gtg tac gcc gag acc aag cac ttc ctc tac tcc tca ggc     1008
Cys Pro Pro Val Tyr Ala Glu Thr Lys His Phe Leu Tyr Ser Ser Gly
                325                 330                 335

gac aag gag cag ctg cgg ccc tcc ttc cta ctc agc tct ctg agg ccc     1056
Asp Lys Glu Gln Leu Arg Pro Ser Phe Leu Leu Ser Ser Leu Arg Pro
            340                 345                 350

agc ctg act ggc gct cgg agg ctc gtg gag acc atc ttt ctg ggt tcc     1104
Ser Leu Thr Gly Ala Arg Arg Leu Val Glu Thr Ile Phe Leu Gly Ser
        355                 360                 365

agg ccc tgg atg cca ggg act ccc cgc agg ttg ccc cgc ctg ccc cag     1152
Arg Pro Trp Met Pro Gly Thr Pro Arg Arg Leu Pro Arg Leu Pro Gln
    370                 375                 380

cgc tac tgg caa atg cgg ccc ctg ttt ctg gag ctg ctt ggg aac cac     1200
Arg Tyr Trp Gln Met Arg Pro Leu Phe Leu Glu Leu Leu Gly Asn His
385                 390                 395                 400

gcg cag tgc ccc tac ggg gtg ctc ctc aag acg cac tgc ccg ctg cga     1248
Ala Gln Cys Pro Tyr Gly Val Leu Leu Lys Thr His Cys Pro Leu Arg
                405                 410                 415

gct gcg gtc acc cca gca gcc ggt gtc tgt gcc cgg gag aag ccc cag     1296
Ala Ala Val Thr Pro Ala Ala Gly Val Cys Ala Arg Glu Lys Pro Gln
            420                 425                 430

ggc tct gtg gcg gcc ccc gag gag gag gac aca gac ccc cgt cgc ctg     1344
Gly Ser Val Ala Ala Pro Glu Glu Glu Asp Thr Asp Pro Arg Arg Leu
        435                 440                 445

gtg cag ctg ctc cgc cag cac agc agc ccc tgg cag gtg tac ggc ttc     1392
Val Gln Leu Leu Arg Gln His Ser Ser Pro Trp Gln Val Tyr Gly Phe
    450                 455                 460

gtg cgg gcc tgc ctg cgc cgg ctg gtg ccc cca ggc ctc tgg ggc tcc     1440
Val Arg Ala Cys Leu Arg Arg Leu Val Pro Pro Gly Leu Trp Gly Ser
465                 470                 475                 480
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agg cac aac gaa cgc cgc ttc ctc agg aac acc aag aag ttc atc tcc     1488
Arg His Asn Glu Arg Arg Phe Leu Arg Asn Thr Lys Lys Phe Ile Ser
                485                 490                 495

ctg ggg aag cat gcc aag ctc tcg ctg cag gag ctg acg tgg aag atg     1536
Leu Gly Lys His Ala Lys Leu Ser Leu Gln Glu Leu Thr Trp Lys Met
            500                 505                 510

agc gtg cgg gac tgc gct tgg ctg cgc agg agc cca ggg gtt ggc tgt     1584
Ser Val Arg Asp Cys Ala Trp Leu Arg Arg Ser Pro Gly Val Gly Cys
        515                 520                 525

gtt ccg gcc gca gag cac cgt ctg cgt gag gag atc ctg gcc aag ttc     1632
Val Pro Ala Ala Glu His Arg Leu Arg Glu Glu Ile Leu Ala Lys Phe
    530                 535                 540

ctg cac tgg ctg atg agt gtg tac gtc gtc gag ctg ctc agg tct ttc     1680
Leu His Trp Leu Met Ser Val Tyr Val Val Glu Leu Leu Arg Ser Phe
545                 550                 555                 560

ttt tat gtc acg gag acc acg ttt caa aag aac agg ctc ttt ttc tac     1728
Phe Tyr Val Thr Glu Thr Thr Phe Gln Lys Asn Arg Leu Phe Phe Tyr
                565                 570                 575

cgg aag agt gtc tgg agc aag ttg caa agc att gga atc aga cag cac     1776
Arg Lys Ser Val Trp Ser Lys Leu Gln Ser Ile Gly Ile Arg Gln His
            580                 585                 590

ttg aag agg gtg cag ctg cgg gag ctg tcg gaa gca gag gtc agg cag     1824
Leu Lys Arg Val Gln Leu Arg Glu Leu Ser Glu Ala Glu Val Arg Gln
        595                 600                 605

cat cgg gaa gcc agg ccc gcc ctg ctg acg tcc aga ctc cgc ttc atc     1872
His Arg Glu Ala Arg Pro Ala Leu Leu Thr Ser Arg Leu Arg Phe Ile
    610                 615                 620

ccc aag cct gac ggg ctg cgg ccg att gtg aac atg gac tac gtc gtg     1920
Pro Lys Pro Asp Gly Leu Arg Pro Ile Val Asn Met Asp Tyr Val Val
625                 630                 635                 640

gga gcc aga acg ttc cgc aga gaa aag agg gcc gag cgt ctc acc tcg     1968
Gly Ala Arg Thr Phe Arg Arg Glu Lys Arg Ala Glu Arg Leu Thr Ser
                645                 650                 655

agg gtg aag gca ctg ttc agc gtg ctc aac tac gag cgg gcg cgg cgc     2016
Arg Val Lys Ala Leu Phe Ser Val Leu Asn Tyr Glu Arg Ala Arg Arg
            660                 665                 670

ccc ggc ctc ctg ggc gcc tct gtg ctg ggc ctg gac gat atc cac agg     2064
Pro Gly Leu Leu Gly Ala Ser Val Leu Gly Leu Asp Asp Ile His Arg
        675                 680                 685

gcc tgg cgc acc ttc gtg ctg cgt gtg cgg gcc cag gac ccg ccg cct     2112
Ala Trp Arg Thr Phe Val Leu Arg Val Arg Ala Gln Asp Pro Pro Pro
    690                 695                 700

gag ctg tac ttt gtc aag gtg gat gtg acg ggc gcg tac gac acc atc     2160
Glu Leu Tyr Phe Val Lys Val Asp Val Thr Gly Ala Tyr Asp Thr Ile
705                 710                 715                 720

ccc cag gac agg ctc acg gag gtc atc gcc agc atc atc aaa ccc cag     2208
Pro Gln Asp Arg Leu Thr Glu Val Ile Ala Ser Ile Ile Lys Pro Gln
                725                 730                 735
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aac acg tac tgc gtg cgt cgg tat gcc gtg gtc cag aag gcc gcc cat     2256
Asn Thr Tyr Cys Val Arg Arg Tyr Ala Val Val Gln Lys Ala Ala His
            740                 745                 750

ggg cac gtc cgc aag gcc ttc aag agc cac gtc tct acc ttg aca gac     2304
Gly His Val Arg Lys Ala Phe Lys Ser His Val Ser Thr Leu Thr Asp
        755                 760                 765

ctc cag ccg tac atg cga cag ttc gtg gct cac ctg cag gag acc agc     2352
Leu Gln Pro Tyr Met Arg Gln Phe Val Ala His Leu Gln Glu Thr Ser
    770                 775                 780

ccg ctg agg gat gcc gtc gtc atc gag cag agc tcc tcc ctg aat gag     2400
Pro Leu Arg Asp Ala Val Val Ile Glu Gln Ser Ser Ser Leu Asn Glu
785                 790                 795                 800

gcc agc agt ggc ctc ttc gac gtc ttc cta cgc ttc atg tgc cac cac     2448
Ala Ser Ser Gly Leu Phe Asp Val Phe Leu Arg Phe Met Cys His His
                805                 810                 815

gcc gtg cgc atc agg ggc aag tcc tac gtc cag tgc cag ggg atc ccg     2496
Ala Val Arg Ile Arg Gly Lys Ser Tyr Val Gln Cys Gln Gly Ile Pro
            820                 825                 830

cag ggc tcc atc ctc tcc acg ctg ctc tgc agc ctg tgc tac ggc gac     2544
Gln Gly Ser Ile Leu Ser Thr Leu Leu Cys Ser Leu Cys Tyr Gly Asp
        835                 840                 845

atg gag aac aag ctg ttt gcg ggg att cgg cgg gac ggg ctg ctc ctg     2592
Met Glu Asn Lys Leu Phe Ala Gly Ile Arg Arg Asp Gly Leu Leu Leu
    850                 855                 860

cgt ttg gtg gat gat ttc ttg ttg gtg aca cct cac ctc acc cac gcg     2640
Arg Leu Val Asp Asp Phe Leu Leu Val Thr Pro His Leu Thr His Ala
865                 870                 875                 880

aaa acc ttc ctc agg acc ctg gtc cga ggt gtc cct gag tat ggc tgc     2688
Lys Thr Phe Leu Arg Thr Leu Val Arg Gly Val Pro Glu Tyr Gly Cys
                885                 890                 895

gtg gtg aac ttg cgg aag aca gtg gtg aac ttc cct gta gaa gac gag     2736
Val Val Asn Leu Arg Lys Thr Val Val Asn Phe Pro Val Glu Asp Glu
            900                 905                 910

gcc ctg ggt ggc acg gct ttt gtt cag atg ccg gcc cac ggc cta ttc     2784
Ala Leu Gly Gly Thr Ala Phe Val Gln Met Pro Ala His Gly Leu Phe
        915                 920                 925

ccc tgg tgc ggc ctg ctg ctg gat acc cgg acc ctg gag gtg cag agc     2832
Pro Trp Cys Gly Leu Leu Leu Asp Thr Arg Thr Leu Glu Val Gln Ser
    930                 935                 940

gac tac tcc agc tat gcc cgg acc tcc atc aga gcc agt ctc acc ttc     2880
Asp Tyr Ser Ser Tyr Ala Arg Thr Ser Ile Arg Ala Ser Leu Thr Phe
945                 950                 955                 960

aac cgc ggc ttc aag gct ggg agg aac atg cgt cgc aaa ctc ttt ggg     2928
Asn Arg Gly Phe Lys Ala Gly Arg Asn Met Arg Arg Lys Leu Phe Gly
                965                 970                 975

gtc ttg cgg ctg aag tgt cac agc ctg ttt ctg gat ttg cag gtg aac     2976
Val Leu Arg Leu Lys Cys His Ser Leu Phe Leu Asp Leu Gln Val Asn
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            980                 985                 990

agc ctc cag acg gtg tgc acc aac  atc tac aag atc ctc  ctg ctg cag   3024
Ser Leu Gln Thr Val Cys Thr Asn  Ile Tyr Lys Ile Leu  Leu Leu Gln
        995                 1000                1005

gcg tac  agg ttt cac gca tgt  gtg ctg cag ctc cca  ttt cat cag      3069
Ala Tyr  Arg Phe His Ala Cys  Val Leu Gln Leu Pro  Phe His Gln
    1010                1015                1020

caa gtt  tgg aag aac ccc aca  ttt ttc ctg cgc gtc  atc tct gac      3114
Gln Val  Trp Lys Asn Pro Thr  Phe Phe Leu Arg Val  Ile Ser Asp
    1025                1030                1035

acg gcc  tcc ctc tgc tac tcc  atc ctg aaa gcc aag  aac gca ggg      3159
Thr Ala  Ser Leu Cys Tyr Ser  Ile Leu Lys Ala Lys  Asn Ala Gly
    1040                1045                1050

atg tcg  ctg ggg gcc aag ggc  gcc gcc ggc cct ctg  ccc tcc gag      3204
Met Ser  Leu Gly Ala Lys Gly  Ala Ala Gly Pro Leu  Pro Ser Glu
    1055                1060                1065

gcc gtg  cag tgg ctg tgc cac  caa gca ttc ctg ctc  aag ctg act      3249
Ala Val  Gln Trp Leu Cys His  Gln Ala Phe Leu Leu  Lys Leu Thr
    1070                1075                1080

cga cac  cgt gtc acc tac gtg  cca ctc ctg ggg tca  ctc agg aca      3294
Arg His  Arg Val Thr Tyr Val  Pro Leu Leu Gly Ser  Leu Arg Thr
    1085                1090                1095

gcc cag  acg cag ctg agt cgg  aag ctc ccg ggg acg  acg ctg act      3339
Ala Gln  Thr Gln Leu Ser Arg  Lys Leu Pro Gly Thr  Thr Leu Thr
    1100                1105                1110

gcc ctg  gag gcc gca gcc aac  ccg gca ctg ccc tca  gac ttc aag      3384
Ala Leu  Glu Ala Ala Ala Asn  Pro Ala Leu Pro Ser  Asp Phe Lys
    1115                1120                1125

acc atc  ctg gac tga                                             3399
Thr Ile  Leu Asp
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            20                  25                  30

Pro Gln Gly Trp Arg Leu Val Gln Arg Gly Asp Pro Ala Ala Phe Arg
        35                  40                  45

Ala Leu Val Ala Gln Cys Leu Val Cys Val Pro Trp Asp Ala Arg Pro
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    50                  55                  60

Pro Pro Ala Ala Pro Ser Phe Arg Gln Val Ser Cys Leu Lys Glu Leu
65                  70                  75                  80

Val Ala Arg Val Leu Gln Arg Leu Cys Glu Arg Gly Ala Lys Asn Val
                85                  90                  95

Leu Ala Phe Gly Phe Ala Leu Leu Asp Gly Ala Arg Gly Gly Pro Pro
            100                 105                 110

Glu Ala Phe Thr Thr Ser Val Arg Ser Tyr Leu Pro Asn Thr Val Thr
        115                 120                 125

Asp Ala Leu Arg Gly Ser Gly Ala Trp Gly Leu Leu Leu Arg Arg Val
    130                 135                 140

Gly Asp Asp Val Leu Val His Leu Leu Ala Arg Cys Ala Leu Phe Val
145                 150                 155                 160

Leu Val Ala Pro Ser Cys Ala Tyr Gln Val Cys Gly Pro Pro Leu Tyr
                165                 170                 175

Gln Leu Gly Ala Ala Thr Gln Ala Arg Pro Pro Pro His Ala Ser Gly
            180                 185                 190

Pro Arg Arg Arg Leu Gly Cys Glu Arg Ala Trp Asn His Ser Val Arg
        195                 200                 205

Glu Ala Gly Val Pro Leu Gly Leu Pro Ala Pro Gly Ala Arg Arg Arg
    210                 215                 220

Gly Gly Ser Ala Ser Arg Ser Leu Pro Leu Pro Lys Arg Pro Arg Arg
225                 230                 235                 240

Gly Ala Ala Pro Glu Pro Glu Arg Thr Pro Val Gly Gln Gly Ser Trp
                245                 250                 255

Ala His Pro Gly Arg Thr Arg Gly Pro Ser Asp Arg Gly Phe Cys Val
            260                 265                 270

Val Ser Pro Ala Arg Pro Ala Glu Glu Ala Thr Ser Leu Glu Gly Ala
        275                 280                 285

Leu Ser Gly Thr Arg His Ser His Pro Ser Val Gly Arg Gln His His
    290                 295                 300
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Ala Gly Pro Pro Ser Thr Ser Arg Pro Pro Arg Pro Trp Asp Thr Pro
305 310 315 320

Cys Pro Pro Val Tyr Ala Glu Thr Lys His Phe Leu Tyr Ser Ser Gly
325 330 335

Asp Lys Glu Gln Leu Arg Pro Ser Phe Leu Leu Ser Ser Leu Arg Pro
340 345 350

Ser Leu Thr Gly Ala Arg Arg Leu Val Glu Thr Ile Phe Leu Gly Ser
355 360 365

Arg Pro Trp Met Pro Gly Thr Pro Arg Arg Leu Pro Arg Leu Pro Gln
370 375 380

Arg Tyr Trp Gln Met Arg Pro Leu Phe Leu Glu Leu Leu Gly Asn His
385 390 395 400

Ala Gln Cys Pro Tyr Gly Val Leu Leu Lys Thr His Cys Pro Leu Arg
405 410 415

Ala Ala Val Thr Pro Ala Ala Gly Val Cys Ala Arg Glu Lys Pro Gln
420 425 430

Gly Ser Val Ala Ala Pro Glu Glu Glu Asp Thr Asp Pro Arg Arg Leu
435 440 445

Val Gln Leu Leu Arg Gln His Ser Ser Pro Trp Gln Val Tyr Gly Phe
450 455 460

Val Arg Ala Cys Leu Arg Arg Leu Val Pro Pro Gly Leu Trp Gly Ser
465 470 475 480

Arg His Asn Glu Arg Arg Phe Leu Arg Asn Thr Lys Lys Phe Ile Ser
485 490 495

Leu Gly Lys His Ala Lys Leu Ser Leu Gln Glu Leu Thr Trp Lys Met
500 505 510

Ser Val Arg Asp Cys Ala Trp Leu Arg Arg Ser Pro Gly Val Gly Cys
515 520 525

Val Pro Ala Ala Glu His Arg Leu Arg Glu Glu Ile Leu Ala Lys Phe
530 535 540

Leu His Trp Leu Met Ser Val Tyr Val Val Glu Leu Leu Arg Ser Phe
545 550 555 560

```
Phe Tyr Val Thr Glu Thr Thr Phe Gln Lys Asn Arg Leu Phe Phe Tyr
                565                 570                 575

Arg Lys Ser Val Trp Ser Lys Leu Gln Ser Ile Gly Ile Arg Gln His
            580                 585                 590

Leu Lys Arg Val Gln Leu Arg Glu Leu Ser Glu Ala Glu Val Arg Gln
        595                 600                 605

His Arg Glu Ala Arg Pro Ala Leu Leu Thr Ser Arg Leu Arg Phe Ile
    610                 615                 620

Pro Lys Pro Asp Gly Leu Arg Pro Ile Val Asn Met Asp Tyr Val Val
625                 630                 635                 640

Gly Ala Arg Thr Phe Arg Arg Glu Lys Arg Ala Glu Arg Leu Thr Ser
                645                 650                 655

Arg Val Lys Ala Leu Phe Ser Val Leu Asn Tyr Glu Arg Ala Arg Arg
            660                 665                 670

Pro Gly Leu Leu Gly Ala Ser Val Leu Gly Leu Asp Asp Ile His Arg
        675                 680                 685

Ala Trp Arg Thr Phe Val Leu Arg Val Arg Ala Gln Asp Pro Pro Pro
    690                 695                 700

Glu Leu Tyr Phe Val Lys Val Asp Val Thr Gly Ala Tyr Asp Thr Ile
705                 710                 715                 720

Pro Gln Asp Arg Leu Thr Glu Val Ile Ala Ser Ile Ile Lys Pro Gln
                725                 730                 735

Asn Thr Tyr Cys Val Arg Arg Tyr Ala Val Val Gln Lys Ala Ala His
            740                 745                 750

Gly His Val Arg Lys Ala Phe Lys Ser His Val Ser Thr Leu Thr Asp
        755                 760                 765

Leu Gln Pro Tyr Met Arg Gln Phe Val Ala His Leu Gln Glu Thr Ser
    770                 775                 780

Pro Leu Arg Asp Ala Val Val Ile Glu Gln Ser Ser Ser Leu Asn Glu
785                 790                 795                 800

Ala Ser Ser Gly Leu Phe Asp Val Phe Leu Arg Phe Met Cys His His
                805                 810                 815
```

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Ala Val Arg Ile Arg Gly Lys Ser Tyr Val Gln Cys Gln Gly Ile Pro
            820                 825                 830

Gln Gly Ser Ile Leu Ser Thr Leu Leu Cys Ser Leu Cys Tyr Gly Asp
        835                 840                 845

Met Glu Asn Lys Leu Phe Ala Gly Ile Arg Arg Asp Gly Leu Leu Leu
    850                 855                 860

Arg Leu Val Asp Asp Phe Leu Leu Val Thr Pro His Leu Thr His Ala
865                 870                 875                 880

Lys Thr Phe Leu Arg Thr Leu Val Arg Gly Val Pro Glu Tyr Gly Cys
                885                 890                 895

Val Val Asn Leu Arg Lys Thr Val Val Asn Phe Pro Val Glu Asp Glu
            900                 905                 910

Ala Leu Gly Gly Thr Ala Phe Val Gln Met Pro Ala His Gly Leu Phe
        915                 920                 925

Pro Trp Cys Gly Leu Leu Leu Asp Thr Arg Thr Leu Glu Val Gln Ser
    930                 935                 940

Asp Tyr Ser Ser Tyr Ala Arg Thr Ser Ile Arg Ala Ser Leu Thr Phe
945                 950                 955                 960

Asn Arg Gly Phe Lys Ala Gly Arg Asn Met Arg Arg Lys Leu Phe Gly
                965                 970                 975

Val Leu Arg Leu Lys Cys His Ser Leu Phe Leu Asp Leu Gln Val Asn
            980                 985                 990

Ser Leu Gln Thr Val Cys Thr Asn  Ile Tyr Lys Ile Leu  Leu Leu Gln
        995                 1000                1005

Ala Tyr  Arg Phe His Ala Cys  Val Leu Gln Leu Pro  Phe His Gln
    1010                1015                1020

Gln Val  Trp Lys Asn Pro Thr  Phe Phe Leu Arg Val  Ile Ser Asp
    1025                1030                1035

Thr Ala  Ser Leu Cys Tyr Ser  Ile Leu Lys Ala Lys  Asn Ala Gly
    1040                1045                1050

Met Ser  Leu Gly Ala Lys Gly  Ala Ala Gly Pro Leu  Pro Ser Glu
```

1055 1060 1065

Ala Val Gln Trp Leu Cys His Gln Ala Phe Leu Leu Lys Leu Thr
1070 1075 1080

Arg His Arg Val Thr Tyr Val Pro Leu Leu Gly Ser Leu Arg Thr
1085 1090 1095

Ala Gln Thr Gln Leu Ser Arg Lys Leu Pro Gly Thr Thr Leu Thr
1100 1105 1110

Ala Leu Glu Ala Ala Ala Asn Pro Ala Leu Pro Ser Asp Phe Lys
1115 1120 1125

Thr Ile Leu Asp
1130

<210> 5
<211> 1149
<212> DNA
<213> Artificial

<220>
<223> A polynucleotide encoding an inactive variant of MAPKAPK3 (SEQ ID NO:2) which amino acid residues at positions 201 and 313 are both replaced to alanine from threonine

<400> 5
atggatggtg aaacagcaga ggagcagggg ggccctgtgc ccccgccagt tgcacccggc 60

ggacccggct tgggcggtgc tccgggggggg cggcgggagc ccaagaagta cgcagtgacc 120

gacgactacc agttgtccaa gcaggtgctg ggcctgggtg tgaacggcaa agtgctggag 180

tgcttccatc ggcgcactgg acagaagtgt gccctgaagc tcctgtatga cagccccaag 240

gcccggcagg aggtagacca tcactggcag gcttctggcg gcccccatat tgtctgcatc 300

ctggatgtgt atgagaacat gcaccatggc aagcgctgtc tcctcatcat catggaatgc 360

atggaaggtg gtgagttgtt cagcaggatt caggagcgtg gcgaccaggc tttcactgag 420

agagaagctg cagagataat gcgggatatt ggcactgcca tccagtttct gcacagccat 480

aacattgccc accgagatgt caagcctgaa aacctactct acacatctaa ggagaaagac 540

gcagtgctta agctcaccga ttttggcttt gctaaggaga ccacccaaaa tgccctgcag 600

gccccctgct atactcccta ttatgtggcc cctgaggtcc tgggtccaga gaagtatgac 660

aagtcatgtg acatgtggtc cctgggtgtc atcatgtaca tcctcctttg tggcttccca 720

cccttctact ccaacacggg ccaggccatc tccccgggga tgaagaggag gattcgcctg 780

ggccagtacg gcttccccaa tcctgagtgg tcagaagtct ctgaggatgc caagcagctg 840

atccgcctcc tgttgaagac agaccccaca gagaggctga ccatcactca gttcatgaac 900

caccctgga tcaaccaatc gatggtagtg ccacaggccc cactccacac ggcccgagtg 960

ctgcaggagg acaaagacca ctgggacgaa gtcaaggagg agatgaccag tgccttggcc 1020

actatgcggg tagactacga ccaggtgaag atcaaggacc tgaagacctc taacaaccgg 1080

ctcctcaaca agaggagaaa aaagcaggca ggcagctcct ctgcctcaca gggctgcaac 1140

aaccagtag 1149

<210> 6
<211> 382
<212> PRT
<213> Artificial

<220>
<223> An inactive variant of MAPKAPK3 (SEQ ID NO:2) which amino acid residues at positions 201 and 313 are both replaced to alanine from threonine

<400> 6

Met Asp Gly Glu Thr Ala Glu Glu Gln Gly Gly Pro Val Pro Pro Pro
1 5 10 15

Val Ala Pro Gly Gly Pro Gly Leu Gly Gly Ala Pro Gly Gly Arg Arg
20 25 30

Glu Pro Lys Lys Tyr Ala Val Thr Asp Asp Tyr Gln Leu Ser Lys Gln
35 40 45

Val Leu Gly Leu Gly Val Asn Gly Lys Val Leu Glu Cys Phe His Arg
50 55 60

Arg Thr Gly Gln Lys Cys Ala Leu Lys Leu Leu Tyr Asp Ser Pro Lys
65 70 75 80

Ala Arg Gln Glu Val Asp His His Trp Gln Ala Ser Gly Gly Pro His
85 90 95

Ile Val Cys Ile Leu Asp Val Tyr Glu Asn Met His His Gly Lys Arg
100 105 110

Cys Leu Leu Ile Ile Met Glu Cys Met Glu Gly Gly Glu Leu Phe Ser
115 120 125

Arg Ile Gln Glu Arg Gly Asp Gln Ala Phe Thr Glu Arg Glu Ala Ala
130 135 140

Glu Ile Met Arg Asp Ile Gly Thr Ala Ile Gln Phe Leu His Ser His
145 150 155 160

```
Asn Ile Ala His Arg Asp Val Lys Pro Glu Asn Leu Leu Tyr Thr Ser
                165                 170                 175

Lys Glu Lys Asp Ala Val Leu Lys Leu Thr Asp Phe Gly Phe Ala Lys
            180                 185                 190

Glu Thr Thr Gln Asn Ala Leu Gln Ala Pro Cys Tyr Thr Pro Tyr Tyr
        195                 200                 205

Val Ala Pro Glu Val Leu Gly Pro Glu Lys Tyr Asp Lys Ser Cys Asp
    210                 215                 220

Met Trp Ser Leu Gly Val Ile Met Tyr Ile Leu Leu Cys Gly Phe Pro
225                 230                 235                 240

Pro Phe Tyr Ser Asn Thr Gly Gln Ala Ile Ser Pro Gly Met Lys Arg
                245                 250                 255

Arg Ile Arg Leu Gly Gln Tyr Gly Phe Pro Asn Pro Glu Trp Ser Glu
            260                 265                 270

Val Ser Glu Asp Ala Lys Gln Leu Ile Arg Leu Leu Leu Lys Thr Asp
        275                 280                 285

Pro Thr Glu Arg Leu Thr Ile Thr Gln Phe Met Asn His Pro Trp Ile
    290                 295                 300

Asn Gln Ser Met Val Val Pro Gln Ala Pro Leu His Thr Ala Arg Val
305                 310                 315                 320

Leu Gln Glu Asp Lys Asp His Trp Asp Glu Val Lys Glu Glu Met Thr
                325                 330                 335

Ser Ala Leu Ala Thr Met Arg Val Asp Tyr Asp Gln Val Lys Ile Lys
            340                 345                 350

Asp Leu Lys Thr Ser Asn Asn Arg Leu Leu Asn Lys Arg Arg Lys Lys
        355                 360                 365

Gln Ala Gly Ser Ser Ser Ala Ser Gln Gly Cys Asn Asn Gln
    370                 375                 380
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<210> 7
<211> 1149
<212> DNA
<213> Artificial

<220>

<223> A polynucleotide encoding an active variant of MAPKAPK3 (SEQ ID NO:2) which amino acid residues at positions 201 and 313 are both replaced to glutamic acid from threonine

<400> 7

atggatggtg aaacagcaga ggagcagggg ggccctgtgc ccccgccagt tgcacccggc 60

ggacccggct tgggcggtgc tccgggggggg cggcgggagc ccaagaagta cgcagtgacc 120

gacgactacc agttgtccaa gcaggtgctg ggcctgggtg tgaacggcaa agtgctggag 180

tgcttccatc ggcgcactgg acagaagtgt gccctgaagc tcctgtatga cagccccaag 240

gcccggcagg aggtagacca tcactggcag gcttctggcg gcccccatat tgtctgcatc 300

ctggatgtgt atgagaacat gcaccatggc aagcgctgtc tcctcatcat catggaatgc 360

atggaaggtg gtgagttgtt cagcaggatt caggagcgtg gcgaccaggc tttcactgag 420

agagaagctg cagagataat gcgggatatt ggcactgcca tccagtttct gcacagccat 480

aacattgccc accgagatgt caagcctgaa aacctactct acacatctaa ggagaaagac 540

gcagtgctta agctcaccga ttttggcttt gctaaggaga ccacccaaaa tgccctgcag 600

gagccctgct atactcccta ttatgtggcc cctgaggtcc tgggtccaga gaagtatgac 660

aagtcatgtg acatgtggtc cctgggtgtc atcatgtaca tcctcctttg tggcttccca 720

cccttctact ccaacacggg ccaggccatc tccccgggga tgaagaggag gattcgcctg 780

ggccagtacg gcttccccaa tcctgagtgg tcagaagtct ctgaggatgc caagcagctg 840

atccgcctcc tgttgaagac agaccccaca gagaggctga ccatcactca gttcatgaac 900

caccctgga tcaaccaatc gatggtagtg ccacaggagc cactccacac ggcccgagtg 960

ctgcaggagg acaaagacca ctgggacgaa gtcaaggagg agatgaccag tgccttggcc 1020

actatgcggg tagactacga ccaggtgaag atcaaggacc tgaagacctc taacaaccgg 1080

ctcctcaaca agaggagaaa aaagcaggca ggcagctcct ctgcctcaca gggctgcaac 1140

aaccagtag 1149

<210> 8
<211> 382
<212> PRT
<213> Artificial

<220>
<223> An active variant of MAPKAPK3 (SEQ ID NO:2) which amino acid residues at positions 201 and 313 are both replaced to glutamic acid from threonine

<400> 8

Met Asp Gly Glu Thr Ala Glu Glu Gln Gly Gly Pro Val Pro Pro Pro
1 5 10 15

Val Ala Pro Gly Gly Pro Gly Leu Gly Gly Ala Pro Gly Gly Arg Arg

```
            20                  25                  30

Glu Pro Lys Lys Tyr Ala Val Thr Asp Asp Tyr Gln Leu Ser Lys Gln
        35                  40                  45

Val Leu Gly Leu Gly Val Asn Gly Lys Val Leu Glu Cys Phe His Arg
    50                  55                  60

Arg Thr Gly Gln Lys Cys Ala Leu Lys Leu Leu Tyr Asp Ser Pro Lys
65                  70                  75                  80

Ala Arg Gln Glu Val Asp His His Trp Gln Ala Ser Gly Gly Pro His
                85                  90                  95

Ile Val Cys Ile Leu Asp Val Tyr Glu Asn Met His His Gly Lys Arg
            100                 105                 110

Cys Leu Leu Ile Ile Met Glu Cys Met Glu Gly Gly Glu Leu Phe Ser
        115                 120                 125

Arg Ile Gln Glu Arg Gly Asp Gln Ala Phe Thr Glu Arg Glu Ala Ala
    130                 135                 140

Glu Ile Met Arg Asp Ile Gly Thr Ala Ile Gln Phe Leu His Ser His
145                 150                 155                 160

Asn Ile Ala His Arg Asp Val Lys Pro Glu Asn Leu Leu Tyr Thr Ser
                165                 170                 175

Lys Glu Lys Asp Ala Val Leu Lys Leu Thr Asp Phe Gly Phe Ala Lys
            180                 185                 190

Glu Thr Thr Gln Asn Ala Leu Gln Glu Pro Cys Tyr Thr Pro Tyr Tyr
        195                 200                 205

Val Ala Pro Glu Val Leu Gly Pro Glu Lys Tyr Asp Lys Ser Cys Asp
    210                 215                 220

Met Trp Ser Leu Gly Val Ile Met Tyr Ile Leu Leu Cys Gly Phe Pro
225                 230                 235                 240

Pro Phe Tyr Ser Asn Thr Gly Gln Ala Ile Ser Pro Gly Met Lys Arg
                245                 250                 255

Arg Ile Arg Leu Gly Gln Tyr Gly Phe Pro Asn Pro Glu Trp Ser Glu
            260                 265                 270
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Val Ser Glu Asp Ala Lys Gln Leu Ile Arg Leu Leu Leu Lys Thr Asp
        275                 280                 285

Pro Thr Glu Arg Leu Thr Ile Thr Gln Phe Met Asn His Pro Trp Ile
    290                 295                 300

Asn Gln Ser Met Val Val Pro Gln Glu Pro Leu His Thr Ala Arg Val
305                 310                 315                 320

Leu Gln Glu Asp Lys Asp His Trp Asp Glu Val Lys Glu Glu Met Thr
                325                 330                 335

Ser Ala Leu Ala Thr Met Arg Val Asp Tyr Asp Gln Val Lys Ile Lys
            340                 345                 350

Asp Leu Lys Thr Ser Asn Asn Arg Leu Leu Asn Lys Arg Arg Lys Lys
        355                 360                 365

Gln Ala Gly Ser Ser Ser Ala Ser Gln Gly Cys Asn Asn Gln
    370                 375                 380
```

<210> 9
<211> 6
<212> PRT
<213> Artificial

<220>
<223> Partial sequence of TERT (SEQ ID NO:4) , which is highly homologo
us to that of MAPKAPK3 (SEQ ID NO:2)

<400> 9

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Pro Pro Pro Ala Ala Pro
1               5
```

<210> 10
<211> 6
<212> PRT
<213> Artificial

<220>
<223> Partial sequence of MAPKAPK3 (SEQ ID NO:2) , which is highly hom
ologous to that of TERT (SEQ ID NO:4)

<400> 10

```
Pro Pro Pro Val Ala Pro
1               5
```

<210> 11
<211> 6
<212> PRT
<213> Artificial

<220>
<223> Partial sequence of TERT (SEQ ID NO:4) , which is highly homologo
us to that of MAPKAPK3 (SEQ ID NO:2)

<400> 11

Ala Pro Gly Ala Arg Arg
1 5

<210> 12
<211> 6
<212> PRT
<213> Artificial

<220>
<223> Partial sequence of MAPKAPK3 (SEQ ID NO:2) , which is highly hom
ologous to that of TERT (SEQ ID NO:4)

<400> 12

Ala Pro Gly Gly Arg Arg
1 5

<210> 13
<211> 5
<212> PRT
<213> Artificial

<220>
<223> Partial sequence identical in the sequences of TERT (SEQ ID NO:4)
and MAPKAPK3 (SEQ ID NO:2)

<400> 13

Ala Arg Val Leu Gln
1 5